*Review*

# Physical Examination–Indicated Cerclage

## *A Systematic Review and Meta-analysis*

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**OBJECTIVE:** To estimate the effectiveness of physical examination–indicated cerclage in the setting of second-trimester cervical dilatation by systematic review and meta-analysis of published studies.

**DATA SOURCES:** We searched MEDLINE, EMBASE, Scopus, ClinicalTrials.gov, Web of Science, and the Cochrane Library for studies published between 1966 and 2014 that evaluated cervical cerclage for the treatment of cervical insufficiency.

**METHODS OF STUDY SELECTION:** The search yielded 6,314 citations. We included cohort studies and randomized controlled trials comparing cerclage placement with expectant management of women with cervical dilatation between 14 and 27 weeks of gestation. Two investigators independently reviewed each citation for inclusion or exclusion and discordant decisions were arbitrated by a third reviewer. Summary estimates were reported as the mean difference and 95% confidence interval (CI) for continuous variables or relative risk and with 95% CI for dichotomous outcomes. Fixed- and random-effects meta-analysis was used, depending on heterogeneity.

**TABULATION, INTEGRATION, AND RESULTS:** Ten studies met inclusion criteria and were included in the final analysis. One was a randomized controlled trial, two were prospective cohort studies, and the remaining seven were retrospective cohort studies. Of the 757 women, 485 (64%) underwent physical examination–indicated cerclage placement and 272 (36%) were expectantly managed. Cerclage was associated with increased neonatal survival (71% compared with 43%; relative risk 1.65, 95% CI 1.19–2.28) and prolongation of pregnancy (mean difference 33.98 days, 95% CI 17.88–50.08).

**CONCLUSION:** Physical examination–indicated cerclage is associated with a significant increase in neonatal survival and prolongation of pregnancy of approximately 1 month when compared with no such cerclage. The strength of this conclusion is limited by the potential for bias in the included studies.

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Cervical insufficiency, previously referred to as cervical incompetence, has classically been defined as painless dilation of the cervix in the absence of contractions or bleeding in the second trimester.[1] Painless second-trimester cervical dilation is an uncommon finding in the general population occurring in less than 1% of pregnancies.[2] Cerclage for the prevention of pregnancy loss in women with prior second-trimester loss or second-trimester cervical dilatation in the index pregnancy was first reported in the 1950s.[3,4] Cerclage placement in the setting of cervical dilatation has been variably referred to as "physical examination–indicated cerclage," "rescue cerclage," and "emergency cerclage." To date, the benefits of cerclage for this indication are not entirely clear.

The optimal evaluation and management of asymptomatic patients presenting with second-trimester cervical dilatation remain controversial. There is only one randomized controlled trial to date evaluating the use of cerclage in this clinical scenario, and it included only 23 patients, seven of whom were pregnant with twins.[5] Several nonrandomized studies have compared outcomes of women receiving cerclage with those expectantly managed in the setting

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of second-trimester cervical dilatation. Observational studies have inherent limitations, but until a well-designed and adequately powered randomized controlled study is performed, these are the best data available on which to make management decisions. The objective of this review was to systematically review the literature enabling comparison and combination of the results to arrive at the most appropriate conclusion regarding the effectiveness of physical examination–indicated cerclage.

## SOURCES

The methodology conformed to Meta-analysis of Observational Studies in Epidemiology (MOOSE) criteria.[6] MEDLINE, EMBASE, Scopus, ClinicalTrials.gov, Web of Science, and the Cochrane Library were systematically searched using the keyword search terms: "cerclage," "cervical cerclage," "physical examination-indicated cerclage," "rescue cerclage," "emergency cerclage," "cervical incompetence," "cervical insufficiency," "uterine cervix cerclage," "uterine cervix incompetence," "uterine cervix insufficiency," "salvage cerclage," and "cervical salvage cerclage." The search was conducted by an experienced librarian (C.W.). References from relevant research articles and reviews were also reviewed. No attempt was made to search for unpublished studies. Searches were limited to studies in humans in all languages and to publication dates from 1966 to November 2014.

## STUDY SELECTION

For inclusion, studies needed to compare cerclage with no cerclage in women with a physical examination that revealed cervical dilatation of 0.5 cm or greater between 14 and 27 weeks of gestation. Studies evaluating cerclage based on ultrasound findings but with a closed cervix were ineligible. Both prospective and retrospective studies, including abstracts, were included; those without a control group of expectantly managed women were excluded.

Titles and abstracts for all of the identified studies were independently reviewed by two reviewers (R.M.E., L.S.), and the full article was reviewed in further detail when needed to determine if the study met inclusion criteria. Any disagreements were resolved with discussion with a third reviewer (N.S.S.). Data were independently extracted by the two reviewers (R.M.E. and L.S.) using previously prepared data extraction forms and any discrepancies were resolved by discussion with a third reviewer (N.S.S.). Further clarification and additional data were sought from authors when required and attempts were made to obtain patient-level data from authors. The protocol for this review was registered in the PROSPERO International Prospective Register of Systematic Reviews (CRD42014015654).

Statistical analyses were conducted with Review Manager (RevMan) 5.3. Cerclage placement was compared with 114 no cerclage placement, and the primary outcomes of interest were neonatal survival and time from diagnosis to delivery. Additional outcomes included gestational age at delivery, preterm delivery at less than 24 weeks of gestation, delivery between 24 and 28 weeks of gestation, delivery at less than 34 weeks of gestation, intraoperative membrane rupture, cervical laceration, and birth weight.

Meta-analyses were performed with cohort studies and the randomized controlled trial combined given that there was only one randomized trial. The studies were weighted based on the number of participants. The data analysis was completed independently by authors (N.S.S., G.S., V.B.). The completed analyses were then compared, and any difference was resolved with review of the entire data and independent analysis. Statistical heterogeneity between studies was assessed using the Cochrane Q statistic and Higgins $I^2$ statistics. In case of statistically significant heterogeneity ($P$ value of the Cochrane Q statistic $<.1$), the random-effects model of DerSimonian and Laird was used to obtain the pooled relative risk (RR) estimate; otherwise, a fixed-effect models was planned. The summary measures were reported as RRs with 95% confidence intervals (95% CIs).

To further address heterogeneity, it was predetermined that an analysis of the studies deemed to be at the lowest risk of bias would be performed. The quality of each study was evaluated by two investigators (R.M.E. and N.S.S.). The Cochrane tool for assessment of bias was used for the randomized controlled trial and for the cohort studies, assessment for bias was performed using an approach similar to that described by the Cochrane Non-Randomized Study Group.[7] With this approach, differences in baseline characteristics are compared to evaluate for selection bias because the factors determining which group a woman is allocated to are often unknown. The study design and similarity of the treatment and control groups were evaluated to estimate the risk of bias for the following six characteristics: obstetric history, gestational age at diagnosis, cervical dilation at diagnosis, subclinical evidence of infection, antibiotic use, and tocolysis use. If a study reported a statistically significant difference in parity, history of preterm delivery, or second-trimester loss, the potential for bias regarding obstetric history was considered to be high. A difference of greater than 1 week for

**Table 1. Characteristics of the Included Studies**

| Study | Study Design, Location, Time | Participants | Primary Outcome | Inclusion Criteria | Exclusion Criteria |
|---|---|---|---|---|---|
| Olatunbosun et al, 1995[16] | Prospective cohort study, three academic centers in Nigeria, Saudi Arabia, and Canada, 1987–1993 | 22 cerclage, 15 no cerclage | Not stated | Singleton pregnancy (20–27 wk of gestation), cervical dilatation 4 cm or greater, and 50% effaced with visible membranes | Labor, "significant" bleeding, evidence of infection, history of recurrent pregnancy loss, potential cause for 2nd-trimester abortion |
| Morin et al, 1997[17] | Retrospective cohort study, academic center in Canada, 1978–1995 | 53 cerclage, 22 no cerclage | Not stated | Gestational age 16–26 wk with painless cervical dilatation | Evidence of preterm labor |
| Novy et al, 2001[18] (group 2 only) | Retrospective cohort study, academic center in the United States, 1995–1999 | 19 cerclage, 16 no cerclage | Not stated | Gestational age 18–27 wk, cervical dilatation 2–5 cm and 60% or greater effacement with visible membranes | Labor, bleeding, evidence of infection, fetal anomaly, uterine anomaly, poor response to tocolysis, previous cerclage, known medical cause for 2nd-trimester abortion |
| Althuisius et al, 2003[5] | Randomized controlled trial, single academic center in the Netherlands 1995–2000 | 13 cerclage (3 twins), 10 no cerclage (4 twins) | Delivery at less than 34 wk of gestation, compound neonatal morbidity, neonatal survival | Gestational age less than 27 wk with membranes at or beyond the cervical os | Labor, membrane rupture, and evidence of infection |
| Daskalakis et al, 2006[19] | Prospective cohort study, single academic center in Greece, 1999–2005 | 29 cerclage, 17 no cerclage | Time from presentation to delivery | Singleton pregnancy (18–26 wk of gestation), cervical dilatation greater than 2 cm, and membranes at or beyond the external os | Labor, "significant" bleeding, evidence of infection, history of recurrent pregnancy loss, prior preterm birth, prior 2nd-trimester loss or prior termination, potential cause for 2nd-trimester abortion uterine anomalies, and fetal anomalies |
| Pereira et al, 2008[20] | Retrospective cohort study, 10 international centers, 1998–2005 | 152 cerclage, 73 no cerclage | Time from presentation to delivery | Singleton pregnancy (14–25 6/7 wk of gestation), cervical dilatation 1 cm or greater | Ruptured membranes, labor, bleeding, infection, or multiple gestation |
| Stupin et al, 2008[12] | Retrospective cohort study, academic center in Germany, 1989–2005 | 89 cerclage, 72 no cerclage | Time from presentation to delivery, neonatal survival, and birthweight | Gestational age 17–26 wk, cervical dilatation with membrane prolapse | Previous operation of the cervix in the current pregnancy, membrane rupture, or evidence of infection |
| Ventolini et al, 2009[21] | Retrospective cohort study, academic center in the United States, 2003–2005 | 56 cerclage, 12 no cerclage | Not reported | Gestational age 18–23 6/7 wk, cervical dilatation 3–5 cm, and membranes at or beyond below the cervical os | Ruptured membranes, uterine contractions, bleeding, infection, fetal anomaly, or multiple gestation |

(*continued*)

**Table 1. Characteristics of the Included Studies (*continued*)**

| Study | Study Design, Location, Time | Participants | Primary Outcome | Inclusion Criteria | Exclusion Criteria |
|---|---|---|---|---|---|
| Curti et al, 2012[22] | Retrospective cohort study, two academic centers in Italy, 2001–2009 | 37 cerclage, 15 no cerclage | Time from presentation to delivery and neonatal survival | Gestational age of 17–27 wk and cervical dilatation 1 cm or greater | Ruptured membranes, labor, bleeding, infection, cervical dilatation greater than 6 cm, or multiple gestation |
| Aoki et al, 2013[23] | Retrospective cohort study, academic center in Japan, 2000–2012 | 15 cerclage, 20 no cerclage | Not stated | Gestational age of 15–26 6/7 wk and cervical dilatation 1–4 cm | Ruptured membranes, treatment resistant contractions, bleeding, chorioamnionitis, fetal anomalies, or multiple gestation |

gestational age or 1 cm for dilatation at the time of diagnosis, between the cerclage and control groups, was considered to suggest a high risk of bias. If studies reported on markers of inflammation or a history of preterm delivery, a statistically significant difference was considered to suggest a high risk of bias. When tocolysis and antibiotic regimens were stated to be the same for both groups, the potential for treatment bias was considered low; if it was stated to be different, or a statistically significant difference was shown, the potential for treatment bias was considered to be high. If details were not reported, it was unable to be determined.

## RESULTS

The initial search yielded a total of 6,314 titles and abstracts. Of these, 17 met the inclusion criteria, and seven were subsequently excluded for the one of the following reasons: could not feasibly be translated into English,[8,9] did not adequately report results for the control group,[10] appeared to be a duplicate publication,[11,12] only included patients undergoing repeat cerclage,[13] only included twins,[14] or was limited to multiple gestations attempting a delayed interval delivery.[15] Attempts were made to contact all authors to obtain unpublished data. The remaining 10 studies were included in the analysis, resulting in a total of 757 women eligible for a physical examination–indicated cerclage.[5,12,16–23] Of these, 485 (64%) women underwent cerclage placement and 272 (36%) were expectantly managed. Only one of the studies was a randomized controlled trial (23 pregnancies),[5] two were prospective cohort studies,[16,19] and the remaining seven were retrospective cohort studies.[12,17,18,20–23] Characteristics of each study are described in Table 1 and a description of the surgical procedure and associated is provided in Table 2.

For the randomized controlled trial, randomization was organized in balanced blocks and assigned by telephone.[5] The study was at low risk for selection bias or bias with regard to attrition or reporting. Participants and health care providers were not blinded, and all of the women in the cerclage group routinely received perioperative indomethacin; those in the bed rest group did not. All of the women in both groups received 1 g amoxicillin–clavulanic acid intravenously every 6 hours and 500 mg metronidazole intravenously every 8 hours for 1 week. Blinding was not feasible in this study, and the use of indomethacin in the cerclage group does result in a potential for treatment bias. The risk of bias for the cohort studies is shown in Table 3. Three of the nine (33.3%) cohort studies did not demonstrate a high risk of bias in any of the predefined categories,[16,19,21] but for one of these studies,[21] there was insufficient information to evaluate six of the seven elements in the bias table. Pereira et al[20] were the only authors who performed a multivariate analysis to adjust for potential confounders.

The cerclage and expectantly managed groups were similar in regard to maternal age, nulliparity, and history of previous preterm birth. Pereira et al reported significantly higher rates of previous second-trimester loss in the cerclage group compared with the expectantly managed group (45% compared with 18%, $P \leq .01$). When reported, no differences between the groups regarding parity[5,12,16,18,19,22,23] or history of preterm birth[5,16,18–20,23] were reported in any study. Specific characteristics of the study groups are further reported in Table 4. Women in the cerclage group were diagnosed approximately 1 week earlier than the expectant management group (mean difference −1.02 weeks, 95% CI −2.00 to −0.05), but there was no significant difference in the cervical dilatation between the cerclage group and the expectantly

**Table 2. Description of the Intervention and Associated Treatments**

| Study | Intervention | Antibiotics | Tocolysis | Activity |
|---|---|---|---|---|
| Olatunbosun et al, 1995[16] | Observation period: 4–6 h; procedure: steep Trendelenburg tilt and inflated Foley balloon with tip cut or retrograde filling of the bladder used to reduce membranes; cerclage type: modified McDonald; two 1 silk pursestring sutures followed by four 00 silk stay sutures tied over the external os; suture material: silk | Ampicillin or cefoxitin×5 d | Ritodrine intravenous or indomethacin suppository×48 h | Cerclage group: strict bedrest×48 h then discharge to home in 5–6 d and advised to continue pelvic rest; no cerclage group: admitted for bed rest until delivery |
| Morin et al, 1997[17] | Observation period: unspecified; procedure: unspecified; cerclage type: unspecified; suture material: unspecified | Unspecified | Unspecified | Unspecified |
| Novy et al, 2001[18] (group 2 only) | Observation period: 4–24 h, possible tocolysis; procedure: steep Trendelenburg tilt and moist swab used to reduce membranes; cerclage type: modified Shirodkar or McDonald; suture material: Shirodkar: Mersilene tape (5 mm); McDonald: "large nonabsorbable monofilament suture" | Broad-spectrum antibiotics frequently used but regimens unspecified | Various agents frequently used but unspecified | Bed rest in the hospital and then discharged to home and advised to continue bed rest as feasible |
| Althuisius et al, 2003[5] | Observation period: none stated; procedure: steep Trendelenburg tilt and inflated Foley balloon used to reduce membranes; cerclage type: McDonald; suture material: braided polyester thread (metric 8/United States Pharmacopeia 6) | All received 1 g amoxicillin–clavulanic acid intravenously every 6 h and 500 mg metronidazole intravenously every 8 h for 1 wk | Cerclage group only received 100 mg indomethacin suppository 2 h before the procedure and 6 h after the procedure | Inpatient bed rest until 30 wk of gestation |
| Daskalakis et al, 2006[19] | Observation period: 8–24 h; procedure: steep Trendelenburg tilt and moist swab used to reduce membranes; cerclage type: McDonald; suture material: polyester cerclage tape (5 mm) | Cefuroxime and metronidazole intravenous×48 h; 1.5 g erythromycin orally daily×10 d | 100 mg indomethacin suppository twice a d×2 d; 5 mg ritodrine orally every 6 h×2 wk | Bed rest in the hospital×7 d then discharge to home and advised to continue "strict bedrest" to 32 wk and then mobilization with "plenty of rest" until delivery |
| Pereira et al, 2008[20] | Observation period: unspecified; procedure: variable and unspecified; cerclage type: variable and unspecified; suture material: not specified | Regimens not specified | Regimens not specified | Not standardized or specified |

(*continued*)

**Table 2. Description of the Intervention and Associated Treatments (*continued*)**

| Study | Intervention | Antibiotics | Tocolysis | Activity |
|---|---|---|---|---|
| Stupin et al, 2008[12] | Observation period: preferably less than 24 h; procedure: variable and details not specified; cerclage type: 73 McDonald, 14 combination of other methods with fibrin adhesive in cervical canal, 2 Saling (see reference); suture material: unspecified | Regimens not specified | Regimens not specified | Absolute bed rest initially and then relaxed and lifted if asymptomatic |
| Ventolini et al, 2009[21] | Observation period: 24 h; procedure: moist iodine-soaked swab, retrograde filling of the bladder used to reduce membranes, or both; cerclage type: Shirodkar; Suture material: Mersilene tape (5 mm) | None | Cerclage group only received indomethacin×24 h | Discharged to home with pelvic and bed rest |
| Curti et al, 2012[22] | Observation period: at least 24 h; procedure: details not specified; cerclage type: Shirodkar n=36, McDonald n=1; suture material: Mersilene tape (5 mm) | Ampicillin or erythromycin intravenous×7 d | Variable and regimen not specified | Not specified |
| Aoki et al, 2013[23] | Observation period: few hours but less than 24 h; procedure: Trendelenburg but not further described; cerclage type: McDonald n=12, Shirodkar n=2, both n=1; suture material: Mersilene tape (5 mm) | "Broad spectrum"×5 d | All participants received but regimen not specified | Cerclage group 6/15 (40%) were temporarily managed as outpatients; bed rest group were all managed inpatient; details regarding activity were not further described |

managed group (mean difference −0.18 cm, 95% CI −0.34 to 0.17) (Table 4). Markers of inflammation or infection were evaluated in three of the studies[12,22,23] and in one study, a higher leukocyte count was noted in the expectantly managed group compared with the cerclage group (median white blood cell count 9.76 K/microliter compared with 14.73 K/microliter; mean difference 4.97, 95% CI 2.25–7.69).[22] Membranes were visible or prolapsed in all women in all of the included studies with the exception of Pereira et al[20] in which membranes were not visible in 85 of 152 (56%) of the cerclage cases; this was not reported for the expectantly managed group. Three studies compared the degree of membrane prolapse, and there was no significant difference between the cohorts in any study.[12,22,23] Twins were excluded in six studies,[16,19–23] included in two studies,[5,18] and inclusion could not be determined in two studies.[12,17]

The use of amniocentesis, antibiotics, and tocolysis at the time of initial evaluation and management was similar between the two groups (Table 4). Administration of tocolysis was reported in seven studies[5,12,16,18,19,22,23] and was nearly universal with two exceptions. In the study by Curti et al,[22] 34 of 52 (65%) of the women received tocolysis, and in the trial by Althuisius et al,[5] indomethacin was not used in the expectant management group. Only two studies reported on the use of amnioce2ntesis and there was no difference between the groups (12% compared with 8%; RR 1.53, 95% CI 0.68–3.43).[20,22] A sensitivity analysis was performed to evaluate for potential selection bias that could be introduced the use of amniocentesis.

**Table 3. Bias Assessment for Nonrandomized Studies**

| Study | Obstetric History | Gestational Age | Dilatation | Evidence of Infection | Tocolysis | Antibiotics |
|---|---|---|---|---|---|---|
| Olatunbosun et al, 1995[16] | Low | Low | Low | Unable to determine | Low | Low |
| Morin et al, 1997[17] | Unable to determine | Unable to determine | High | Unable to determine | Unable to determine | Unable to determine |
| Novy et al, 2001[18] (group 2 only) | Low | High | Low | Unable to determine | Unable to determine | Unable to determine |
| Daskalakis et al, 2006[19] | Low | Low | Low | Unable to determine | Low | Low |
| Pereira et al, 2008[20] | High | High | Low | Unable to determine | Unable to determine | Unable to determine |
| Stupin et al, 2008[12] | Low | High | High | Low | Unable to determine | Unable to determine |
| Ventolini et al, 2009[21] | Unable to determine | Unable to determine | Unable to determine | Unable to determine | Unable to determine | Unable to determine |
| Curti et al, 2012[22] | Low | High | High | High | Low | Unable to determine |
| Aoki et al, 2013[23] | Low | High | Unable to determine | Low | Unable to determine | Unable to determine |

After excluding the two studies in which amniocentesis was used,[20,22] the primary outcome of neonatal survival was still significantly higher in the cerclage group compared with the expectantly managed group (69.7% compared with 50.3%; RR 1.48, 95% CI 1.06–2.05). Shirodkar cerclage was the primary technique used in two studies[21,22]; the remainder primarily used either a McDonald cerclage[5,12,19,23] or modified McDonald cerclage,[16] and, for three studies, the technique could not be determined.[17,18,20] Management strategies for the study groups are further reported in Table 4 and specific management and interventions for each study are described in Table 2.

The primary outcome of neonatal survival was reported in eight studies.[5,12,16–20,22] Survival was more likely in the cerclage group compared with the expectantly managed group (71% compared with 43%; RR 1.65, 95% CI 1.19–2.28) (Table 5; Fig. 1). Cerclage placement was associated with significant prolongation of pregnancy (mean difference 33.98 days, 95% CI 17.88–50.08) (Fig. 2) and greater gestational age of delivery (mean difference 4.62 weeks, 95% CI 3.89–5.36) (Table 5). Physical examination–indicated cerclage was associated with significant reductions in preterm birth between 24 and 28 weeks of gestation (8% compared with 37%; RR 0.23, 95% CI 0.13–0.41), preterm birth at less than 34 weeks of gestation (50% compared with 82%; RR 0.55, 95% CI 0.38–0.80), and higher birth weight (mean difference 1,028 g, 95% CI 714–1,341) (Table 5).

**Table 4. Characteristics of the Women Included in the Meta-analysis**

| Characteristic | Studies/Participants | Cerclage | Expectant | Effect Estimate* |
|---|---|---|---|---|
| Age (y) | 6/556 | 29.8 | 29.9 | 0.82 (−0.35 to 1.95) |
| Nulliparous | 5/331 | 123/192 (64) | 87/139 (63) | 1.02 (0.87–1.21) |
| Previous preterm birth | 3/306 | 62/196 (32) | 30/110 (27) | 1.16 (0.80–1.68) |
| Gestational age at diagnosis (wk) | 8/614 | 21.7 | 22.8 | **−1.02 (−2.00 to −0.05)** |
| Cervical dilatation at diagnosis (cm) | 6/556 | 3.3 | 3.5 | −0.18 (−0.34 to 0.17) |
| Amniocentesis† | 2/277 | 12/189 (12) | 7/88 (8) | 1.53 (0.68–3.43) |
| Antibiotics† | 9/682 | 271/432 (63) | 182/250 (73) | 0.86 (0.78–1.15) |
| Tocolysis† | 7/389 | 208/224 (93) | 141/165 (85) | 1.02 (0.93–1.13) |

Data are weighted mean or n/N (%) unless otherwise specified.
Bold indicates statistical significance.
* Data are mean difference (95% confidence interval) for rows 1, 4, and 5 and relative risk (95% confidence interval) for rows 2, 3, 6, 7, and 8
† At the time of initial diagnosis and management.

**Table 5. Primary and Secondary Outcomes**

| Studied Outcome | Studies/Participants | Cerclage | Expectant | Effect Estimate* |
|---|---|---|---|---|
| Neonatal survival | 8/657 | 294/413 (71) | 106/244 (43) | **1.66 (1.19–2.30)** |
| Delivery at less than 24 wk of gestation | 3/316 | 51/221 (23) | 31/95 (33) | 0.47 (0.14–1.53) |
| Delivery at 24—28 wk of gestation† | 2/239 | 14/165 (8) | 31/83 (37) | **0.23 (0.13–0.41)** |
| Delivery at less than 34 wk of gestation | 3/316 | 110/221 (50) | 77/94 (82) | **0.55 (0.38–0.80)** |
| Time to delivery (d) | 6/385 | 56.7 | 18.8 | **33.98 (17.88–50.08)** |
| Gestational age at delivery (wk) | 8/643 | 30.6 | 25.2 | **4.62 (3.89–5.36)** |
| Birth weight (g) | 5/331 | 1,714.6 | 829.4 | **1,028 (714–1,341)** |

Data are n/N (%) or weighted mean unless otherwise specified.
Bold indicates statistical significance.
* Data are relative risk (95% confidence interval) for the top four rows and mean difference (95% confidence interval) for the bottom three rows.
† Referent group is women who delivered either before 24 weeks of gestation or after 28 weeks of gestation.

In women undergoing cerclage, the incidence of intraoperative membrane rupture was 4.1% (10 of 246)[5,12,19,21–23] and for cervical laceration was 7.9% (seven of 140)[12,16,17,19]; however, these data were not reported for the control groups. The patients in which intraoperative membrane rupture occurred were included in the treatment group based on the principle of intention to treat for these 10 patients. Olatunbosun also reported one case of intraoperative membrane rupture, but this participant was excluded from the study.[16] No maternal deaths were reported; however, one study reported an intensive care unit admission for sepsis in a cerclage recipient,[20] but this outcome was only specified in one other study.[23] Rates of placental abruption, premature preterm rupture of membranes, and chorioamnionitis were inconsistently and variably reported.

Six of the 10 studies were excluded from the subanalysis of studies with the lowest risk of bias because a high risk of bias was noted in at least one category evaluated (Table 3).[12,17,18,20,22,23] Although the potential for treatment bias in the trial by Althuisius et al was high, the decision was made to include it in the subanalysis because indomethacin in this clinical setting has not been shown to have a significant effect on outcomes.[24] Of the remaining studies, outcome reporting by Ventolini et al[21] was insufficient to permit evaluation of bias for six of the seven categories evaluated so it was excluded. Therefore, the studies by Daskalakis et al, Olatunbosun et al, and Althuisius et al were included in the subanalysis.[5,16,19] In the subanalysis, cerclage was also associated with higher rates of neonatal survival (78% compared with 33%, RR 2.11, 95% CI 1.41–3.55) and prolongation of pregnancy (mean difference 34.00 days, 95% CI 3.11–64.89).

## DISCUSSION

Included articles in this meta-analysis were limited in number and variable in quality and study design. Although differences in our primary outcomes were found, this meta-analysis also underscores the paucity and low quality of existing studies of physical examination–indicated cerclage. Our findings suggest that physical examination–indicated cerclage is associated with significantly but modestly higher rates of neonatal

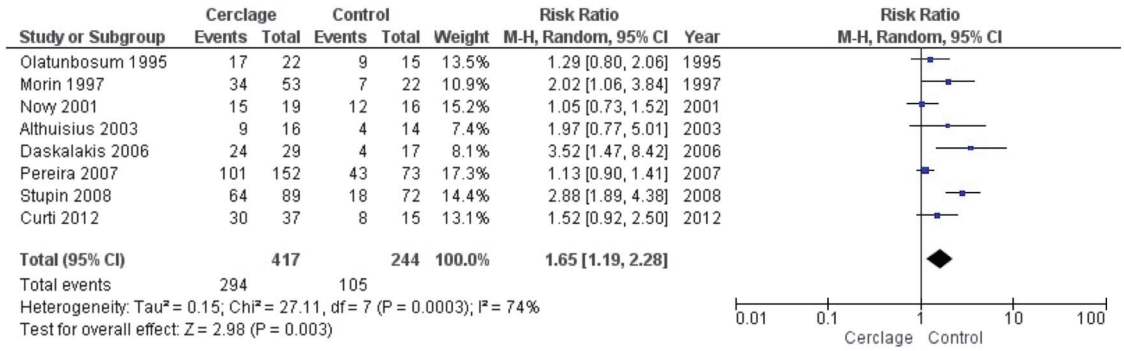


**Fig. 1.** Forest plot for neonatal survival. M-H, Mantel-Haenszel test; CI, confidence interval.
*Ehsanipoor. Physical Examination–Indicated Cerclage. Obstet Gynecol 2015.*

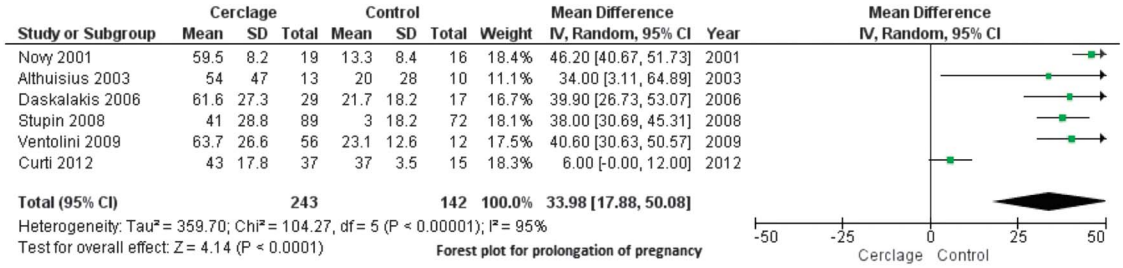


**Fig. 2.** Forest plot for prolongation of pregnancy. SD, standard deviation; IV, independent variable; CI, confidence interval. *Ehsanipoor. Physical Examination–Indicated Cerclage. Obstet Gynecol 2015.*

survival and significant prolongation of pregnancy when compared with no operative intervention. Cerclage was associated with statistically significant favorable outcomes for all secondary outcomes evaluated, except delivery before 24 weeks of gestation.

We could not identify any meta-analysis on the safety and effectiveness of physical examination–indicated cerclage compared with no cerclage. Our results are in agreement with the included studies that had consistent findings. All studies that evaluated time to delivery demonstrated significant prolongation with cerclage.[5,12,18–23] Additionally, the eight studies that evaluated neonatal survival demonstrated higher survival rates with cerclage[5,12,16–20,22]; however, only three were sufficiently powered to demonstrate statistical significance.[12,19,20] Namouz et al[25] recently conducted a review of 34 studies, including case series, evaluating physical examination–indicated cerclage. Neonatal survival rates were similar between our study (72.2%) and those of Namouz et al (81%). Additionally, the mean prolongation of pregnancy and gestational of delivery in our study (53.8 days and 30.5 weeks, respectively) were similar to theirs (56 days and 30.6 weeks of gestation, respectively). We could not identify any case series describing the natural course of expectantly managed pregnancies with second-trimester cervical dilatation. However, our results are similar to those of Vaisbuch et al[26] who reported on women without cervical dilatation but no functional cervical length. The mean prolongation of pregnancy in our study of expectant management (14.1 days) is comparable with the median of 21 days reported by Vaisbuch et al. The slightly shorter interval in our study seems plausible because cervical dilatation was already present. In those who underwent cerclage, the 7.9% rate of cervical laceration and 4.1% rate of intraoperative membrane rupture are consistent with previously reported rates.[27,28]

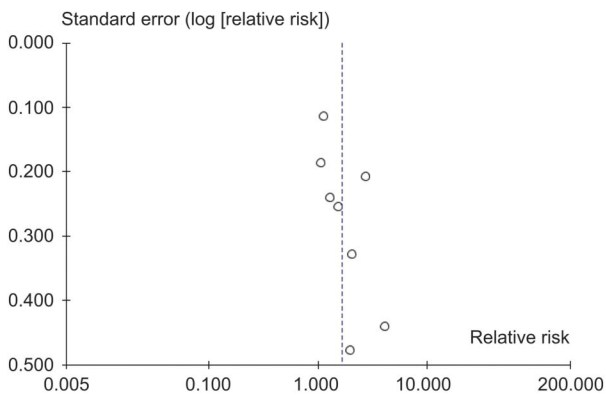


**Fig. 3.** Funnel plot for assessing publication bias. *Ehsanipoor. Physical Examination–Indicated Cerclage. Obstet Gynecol 2015.*

A concern with physical examination–indicated cerclage is that it may prolong pregnancy long enough only to result in an extremely preterm delivery. However, we found that expectant management was associated with a more than fourfold increased risk of delivery between 24 and 28 weeks of gestation. Because the majority of patients in this study were from nonrandomized trials, the potential for bias is strong here because clinicians may have opted for expectant management in patients they deemed to be at higher risk for short-term delivery. Similarly, Aoki et al[23] found that the rate of delivery between 22 and 28 weeks of gestation was 20% in the cerclage group and 80% in the expectantly managed group ($P<.01$). Pereira et al.'s[20] data suggest a potential bimodal distribution of the gestational age of delivery in the cerclage group. This bimodal distribution suggests that there may be a subset of women with a more favorable outcome after cerclage placement and another subset that is likely to deliver early. This may be related to the presence of subclinical infection and may explain why women who have undergone amniocentesis have been shown to have more favorable outcomes.

The strength of this study is that it synthesizes the results of smaller existing studies. Although pooling data from randomized trials is preferred, appraisal and

systematic evaluation of existing observational studies can nonetheless yield important conclusions. Although the quality of the study methods and reporting of these studies varied widely, the results of the subanalysis of the highest quality studies were consistent with the primary findings. Risk of publication bias was assessed by visual inspection of the funnel plot and the symmetric plot suggested no publication bias (Fig. 3).

Study quality was the most obvious limitation. Suboptimal study design can introduce bias in a meta-analysis of observational studies. The potential for selection bias exists with nonrandom allocation. Neither the cerclage nor the expectant group was at an obviously higher risk for poor outcome. Cervical dilatation, prolapsed membranes, obstetric history, evidence of infection, and evaluation with amniocentesis are factors that have been correlated with outcomes of physical examination–indicated cerclage.[29–31] In one study, participants in the cerclage group were more likely to have a history of second-trimester loss[20] and in another, the expectant group had a higher mean leukocyte count.[22] Otherwise, no differences were noted in cervical dilatation, membrane prolapse, or use of amniocentesis. The only significant difference seen was that the mean gestational age for the cerclage group was 22.8 weeks of gestation compared with 21.7 weeks of gestation. Cerclage placement at earlier gestational ages has been associated with improved outcomes in some, but not all studies.[30,31] The possibility of treatment bias exists, and the use of obstetric or neonatal interventions such as fetal monitoring, cesarean delivery, and neonatal resuscitation was not reported. Neonatal outcomes were inconsistently reported and long-term child outcomes were not reported. Despite these limitations, the consistency of the findings of the included studies, subanalysis, and published case series suggests reliability.[25]

In summary, the current literature suggests that physical examination–indicated cerclage is associated with markedly improved outcomes. The quality of these studies is limited, and a randomized controlled trial is warranted as are prospective studies to identify the best candidates for cerclage. Until further evidence is available, physical examination–indicated cerclage should be considered in appropriately selected patients.

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